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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,930	04/25/2001	Paul H. Weigel	5820.603	1177

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EXAMINER	
SPECTOR, LORRAINE	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/842,930	WEIGEL ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,42 and 88-134* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,42 and 88-134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/27/2003 has been entered.

Claims 24, 42 and 88-134 are pending and under consideration.

The rejection of claims under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McCourt et al., Hepatology 30:1276, cited by applicants, for reasons of record is withdrawn in view of the Weigel declaration of 10/27/2003. Applicants have demonstrated reduction to practice of rat HARE presumably having SEQ ID NO: 2 prior to the publication date of McCourt et al. It is noted that the rat HARE so reduced to practice was not sequenced, and that there is no evidence of record that it was "purified to a state capable of being sequenced", and further that there is no reduction to practice of recombinantly produced HARE prior to the publication by McCourt et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 42 and 88-134 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amended and newly introduced claims contain several new limitations that do not find support in the specification as originally filed, nor have applicants pointed out specific support for the new limitations. The limitations that are not supported by the specification as originally filed are: That the protein is "purified to a state capable of being sequenced", and that the protein is ≥76, 80, or 85% identical to SEQ ID NO: 2. No basis for these limitations can be found in the specification as originally filed.

Applicants point to paragraphs [0061] and [0162] of the specification for basis for the new limitations. However, paragraph [0061] merely states that variants with at least 40-90% sequence identity are envisioned, which does not provide basis for 76, 80, or 85%. Paragraph [0162] states that "The cytoplasmic domains of the two HARE proteins are less conserved (25% identical) than their transmembrane (76% identical) or extracellular domains (80%)." However, such does not provide basis for a limitation that two proteins are at least 76% identical overall, nor does it evidence conception that the invention includes proteins which have that amount of identity and retain function. There is no description of the newly introduced limitation, nor does such reasonably flow from the specification as originally filed.

Claims 24, 42 and 88-134 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Even if the new limitations did not constitute new matter, the specification does not provide an adequate written description to support the breadth of the claims. The specification discloses rat and human HARE polypeptides, having two specific sequences, SEQ ID NO: 2 and SEQ ID NO: 25. The written description is not adequate to cover the scope of "mammalian" HARE, nor "mammalian" HARE that is ≥76% identical to SEQ ID NO: 2.

The descriptions of the two HARE from rat and human do not constitute a description of the genus of 'mammalian' HARE, as there is no characteristic structure known to be conserved,

nor is it predictable what the proteins will look like as isolated from other species. It is noted that this rejection was first made in the First Office Action on the Merits, and is now reinstated.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The protein itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In this case, rat and human sequences have been disclosed, however there is no conception of HARE from any other mammalian species.

Therefore, only SEQ ID NO: 2 or SEQ ID NO: 25, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 24, 42, 88-92, 94-97, 99-102, 104-108, 110-114, 116-120, 122-126 and 128-133 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for complete HARE 175 and 300, and fragments of HARE 175, is not enabling for HARE having 76, 80 85 or 90 percent sequence identity with SEQ ID NO: 2. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claimed invention is drawn to mammalian HARE, fragments thereof, and compositions comprising such. The state of the prior art, as cited in the rejections below, is that both human and rat 175 and 300 kD HARE were known and isolated, but had not been cloned. The specification as filed provides little guidance as to how the HARE175 might be altered and still retain function. The working examples include the isolation of the receptor from natural sources, a complete clone of rat HARE 175, and a partial clone of human HARE 175. There are no working examples of alterations of any HARE receptor. Accordingly, it is concluded that it would require undue experimentation to practice the claimed invention in a manner commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24, 42 and 88-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Rejected claims 24, 42 and 88-103 have the limitation that the claimed protein is "purified to a state capable of being sequenced." The term "capable of being sequenced" in the

claims is a relative term which renders the claims indefinite. The term "capable of being sequenced" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Any protein is "capable of being sequenced". In the specification, proteins were variously subjected to N-terminal sequencing, or isolated and digested with trypsin, the fragments sequenced, and then the sequences assembled *in scripto*. It cannot be determined which preparations in the specification are envisioned as meeting the limitation, nor can the metes and bounds of the limitation be determined.

Claims 104-115 state that the protein is "substantially free of other proteins." The term "substantially free of other proteins " in the claims is a relative term which renders the claims indefinite. The term " substantially free of other proteins" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Rejections Over Prior Art

Claim interpretation:

As the metes and bounds of the phrases "capable of being sequenced" and "substantially free of other proteins" cannot be determined, these limitations are not given weight in interpreting the claims.

The recitation that the protein is "recombinant" or which incorporate recombinant production of protein in product-by-process limitations is not being given weight in interpreting the claims. Product by process limitations are proper when they affect the product so produced. However, as the naturally occurring protein would be undistinguishable from recombinantly produced protein, the limitation is not given weight in the pending protein and composition claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24, 42 and 88-134 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yannariello-Brown et al., Glycobiology 7:15, cited by applicants, for reasons of record in the previous Office Action at pages 9-10, as applied to claims 19-27 and 41-47.

As stated in the previous Office Action, Yannariello-Brown et al. disclose the purification of rat liver sinusoidal endothelial cell hyaluronan receptor (title). At page 15, first column, they disclose that both 175 kDa and 300 kDa receptors were isolated. See page 18 for discussion of fractions having activity; those fractions meet the limitation of being 'purified mammalian HARE' as they are purified relative to their naturally obtainable state (see page 49 of the specification wherein this definition is set forth), and also of being compositions, as they were not purified to homogeneity.

The Yannariello-Brown reference is silent with respect to amino acid sequence of the isolated receptors and also with respect to binding of particular antibodies thereto. However, in view of the source, properties, and molecular weights of the disclosed receptors, they appear to be consistent with those of the claims. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. With these conditions, where the

(product or apparatus or method or product by process) seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Applicants traversal of this rejection, filed 10/27/2003 has been fully considered but is not deemed persuasive. Applicants argue that the protein of Yannariello-Brown it was was not pure enough to sequence. This argument has been fully considered but is not deemed persuasive because lane 2 of Figure 5B shows a clearly visible band associated with the activity, said band well separated from other bands of protein. The protein in that band appears to be "substantially free of other proteins", would inherently comprise SEQ ID NO: 2, and would be "capable of being sequenced" by extracting the band from the gel, and either sequencing the N-terminus or digesting with trypsin and then sequencing the fragments, the procedures used by applicants in the instant specification. Applicants are reminded that the phrase "capable of" merely means that it would be *possible* to do so under *some* condition; not that it be easy, or be achievable by a certain process. The Examiner's position is supported by the case law; it has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. See *In re Hutchison*, 69 USPQ 138.

Applicants argument that the protein of Yannariello-Brown et al. would not have met the activity limitation of the claims has been fully considered but is not deemed persuasive. Contrary to applicant's assertion, the legend to Figure 5 clearly states that the SDS-PAGE was run under *non-reducing* conditions. With respect to claims that recited "recombinant" or use product-by-process limitations, these recitations do not imply any material difference in the product; the protein obtained by Yannariello-Brown would not be distinguishable from the same protein produced via recombinant DNA technology.

It remains that the protein of Yannariello-Brown et al. meets the claim limitations. Applicants have neither amended the claims to define over the reference, nor have they provided

evidence to the contrary. Accordingly, the claims remain anticipated or obvious over the disclosure of Yannariello-Brown et al.

Conclusion

No claim is allowed.

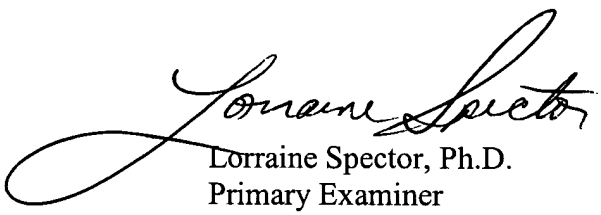
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number will be 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623. ***Effective 1/21/2004, Dr. Kunz' telephone number will be 571-272-0887.***

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228. ***Effective 1/21/2004, Dr. Spector's fax number will be 571-273-0893.***



Lorraine Spector, Ph.D.
Primary Examiner

12/23/2003